CONTRACT CONCEPT REVIEW

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Title: **Toxicity and Carcinogenicity Studies in Rodents**[1]

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I. Purpose

The NTP seeks continued capability to conduct testing and research activities focused on the characterization of toxicologic and carcinogenic potential of chemical, physical, or biological agents. The scope of these activities is too great and the space and personnel needed to conduct these studies exceeds that available at the NIEHS; therefore, studies are carried out through contract mechanisms. The information from NTP's studies helps strengthen the science base used by regulatory agencies in making decisions that protect the public health.

II. Background

The NTP has a long history of conducting general toxicity and carcinogenicity studies in rodents as part of its broad mandate to characterize the toxicity of agents of public health concern. While new approaches to toxicology testing are being explored within the program, these research and testing activities are fundamental to addressing specific deficiencies in the toxicology database for a given agent.

General toxicology and carcinogenicity studies are usually conducted in non-government facilities in accordance with NTP specifications (Specifications for the Conduct of Studies to Evaluate the Toxic and Carcinogenic Potential of Chemical, Biological, and Physical Agents in Laboratory Animals for the National Toxicology Program, October 2006, available at http://ntp.niehs.nih.gov/files/Specifications_2006Oct1.pdf). Although the study designs are flexible, exposures in general toxicology studies typically fall within the range of 14-90 days, and carcinogenicity study designs usually expose animals for up to 2 years. In general, the studies include repeated exposures in mice and/or rats at several dose levels to generate dose-response information, and evaluations for health-related effects including assessments of tissue histopathology, clinical pathology, and sperm motility or measurements of estrous cycle length (standard protocols are available at http://ntp.niehs.nih.gov/go/ba).

In addition to the typical study designs described above, recent designs have included a variety of approaches aimed at more closely approximating human exposure or characterizing specific toxicities. Examples include perinatal exposures, cardiac toxicity endpoints, and RNA collection for gene expression analysis. The work conducted in these contracts over the next 5 years is expected to expand in this direction as a means

[1] As part of its ongoing planning and evaluation, the NTP is bringing this concept to the BSC to get input and endorsement for continuing this type of activity using contract mechanisms. The current contracts are scheduled to end in approximately 4 years.

for understanding better the observed toxicity and carcinogenicity outcomes as well as integrating these data with studies on reproductive, developmental, and/or immune system toxicity conducted within the NTP.

The findings from these studies are reported in NTP's technical report series and are recognized as authoritative by government groups worldwide.

III. Objective

The overall objective of the toxicology and carcinogenicity contracts is to facilitate NTP's effort for characterizing the toxicologic and carcinogenic potential of chemical, physical, or biological agents. These research and testing activities help NTP achieve its goals of testing agents of public health concern, strengthening the science base, and providing information to health regulatory and research agencies, scientific and medical communities, and the public.

IV. Priority

The studies conducted under these contracts are of high priority because they constitute the NTP's core research and testing efforts for carrying out general toxicology studies and chronic bioassays in rodents. While alternative approaches are under development and evaluation, these current efforts are recognized internationally as established and accepted approaches for evaluating the impact of environmental agents in rodent models as a means for identifying potential health hazards for humans.